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*Audrey Boyd*  
*December 20, 2002*

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Attorney Docket No. P31731X1C1

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Anders, *et al.* December 20, 2002  
Serial No.: 10/071,338 Group Art Unit No.: 1652  
Filed: Herewith Examiner: Kathleen Kerr  
For: Isolated 5R Clavams and Methods for Their Manufacture

Assistant Commissioner of Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Applicants submitted a preliminary amendment to the application on February 13, 2002. Preliminary to the examination of this application, applicants respectfully request amendment of the above-identified application as follows:

Please amend the above-identified application as follows:

**In the Claims**

Please cancel claims 38-44.

Please add new claims 45-49.

45. A pharmaceutical composition which is free of one or more of the clavams selected from the group consisting of clavam-2-carboxylate, 2-hydroxymethylclavam, and 2-(3-allyl)clavam comprising clavulanic acid, obtainable by the process comprising the steps of:

(a) disrupting or otherwise making defective a DNA comprising one or more genes specific for 5S clavam biosynthesis in a *Streptomyces*, selected from the group consisting of orfup3 (SEQ ID NO: 2), orfup2 (SEQ ID NO: 3),